

he was of muscular build, with prognathous jaws, a straight thigh, an extremely platymeric tibia, and a thick dolichocephalic skull. The animal-remains found in the cave-earth of other parts of the Cavern, and held by the Author to be contemporaneous with that in the fissure, are those of mid- and late Pleistocene age; and this evidence, together with that derived from the position of the skeleton, the shape of the cranium, and the form and workmanship of the flakes, points to a period towards the close of the Palæolithic or the opening of the Neolithic Age.

MISCELLANEOUS.

The Action of Human Serum on certain Pathogenic Trypanosomes; Action of Arsenious Acid upon Trypanosoma gambiense. By A. LAVERAN.

IN previous notes (1st April, 1902, and 6th July, 1903) I have shown that human serum injected in sufficient doses into mice or rats affected with Nagana, Mal de Caderas, or Surra, caused the Trypanosomes to disappear, at least temporarily, from the greater circulation.

A mouse weighing 20-25 grammes required 0.5 to 1 c.c. of human serum; a rat of 200 gm., 2-3 c.c. of serum or 0.20-0.30 gm. of dry serum in powder.

The Trypanosomes disappear in 24 or 36 hours from the larger circulation, but reappear in general at the end of a few days. Sometimes their disappearance is definitive. The most frequently repeated injections of human serum do nothing more than prolong the life of the animals.

In the month of November, 1903, Drs. Dutton and Todd sent me through Dr. Annett two rats, one infected with *Trypanosoma gambiense*, the other with a *Trypanosoma* of horses from the Gambia. It appeared demonstrated that *Tr. gambiense*, discovered by Forde and Dutton in Gambia, is identical with the *Trypanosoma* described by Castellaini under the name of *Tr. ugandense*, as the pathogenic agent in the disease called "sleeping sickness." The study of this parasite is therefore, from the medical point of view, of great interest.

One might think, *a priori*, that *Tr. gambiense*, which is developed in the blood of man, as in that of many other mammals, would not be influenced by human serum, contrary to that which takes place in the case of the Trypanosomes of Nagana, Surra, and Caderas, diseases against which man is naturally immune. This is precisely the result of my observations. Human serum injected in doses of 0.20-0.30 gm. of the powder, in the case of rats weighing 170 to 200 gm. infected with *Tr. gambiense*, proved entirely inactive.

At the beginning of the infection of rats with *Tr. gambiense*, the Trypanosomes are very rare in the blood, and it happens that after

examinations giving positive results, subsequent examinations yield negative results; but at the end of a month or six weeks the Trypanosomes have established themselves in the blood, and their number is, in general, large enough to enable the action of medicaments to be readily observed; and this is the time to be chosen for experiments with drugs and serums.

Fresh serum of guinea-pig, sheep, and horse proved without action upon *Tr. gambiense*, like human serum; this was to be expected, because the guinea-pig, sheep, and horse can alike be infected with *Tr. gambiense*.

P. Manson tried the treatment of a case of injection by *Trypanosoma* with injections of horse serum, but failed (Brit. Med. Journ. 30 May, 1903); the result might have been foreseen, the horse not being refractory to infection by *Tr. gambiense* (Dutton and Todd, 1st Rep. of the Trypanosomiasis Exped. to Senegambia, 1902, Liverpool, 1903, exper. 87, pl. x.).

This Trypanosome develops unfortunately in the blood of most mammals. I ought, however, to say that the serum of a *Cynocephalus*, apparently naturally immune against *Tr. gambiense*, showed itself as little active as the serum of animals having an admitted susceptibility to this Trypanosome.

It will be well to experiment with the serum of animals with acquired immunity against *Tr. gambiense* and that of animals made hyper-immune, but the results of previous researches in this direction with other pathogenic Trypanosomes (Laveran and Mesnil, "Recherches sur le traitement et la prévention du Nagana," Ann. de l'Institut. Pasteur, Nov. 1902), and of some trials of the curative power of serum of animals with acquired immunity against *Tr. gambiense* itself, leave but small hope of a definitive result of such experiments.

Human serum, inactive against *Tr. gambiense*, has, on the contrary, an evident though feeble action on the *Trypanosoma* of horses in the Gambia. It is now demonstrated that this latter Trypanosome must be completely separated from *Tr. gambiense*, from which it is distinguished by its morphological characters, as well as by its pathogenic action on animals; but at the outset of their researches Dutton and Todd have placed the question of the identity or non-identity of these parasites observed in the same region. Their different reaction with human serum provides a fresh proof in support of their differentiation. Human serum injected in sufficiently large doses into mice and rats having a fair number of the Gambia horse Trypanosomes in their blood, generally causes these Trypanosomes to disappear in 36 or 48 hours; but the parasites do not fail to return.

In the cases where the Trypanosomes are numerous, the injection of human serum can only have for result a diminution of their number. The activity of human serum is, in short, real but more feeble than in the case of Nagana, Surra, and Caderas.

Arsenious acid is the only drug which has given any favourable results in the treatment of Surra and Nagana (*op. cit.*, Ann. de

l'Inst. Pasteur, Nov. 1902); it was therefore of interest to experiment on its efficacy against *Tr. gambiense*.

It results from experiments which I have made on rats that arsenious acid, given in sufficient doses, causes the *Tr. gambiense* to disappear from the greater circulation, at least in a temporary manner, and that it can hasten the cure of Trypanosomiasis in these animals. The efficacious dose is 0.1 mgr. of arsenious acid for every 20 grm. of animal, *i. e.* 1 mgr. for a rat of 200 grm.; below this dose the results are nil or incomplete.

(Note.—This is also the efficacious dose in Nagana, Surra, and Caderas. The solution employed for hypodermic injection has the following composition:—Arsenious acid 1 grm., carbonate of soda 1 grm., distilled water 500 grm.—Laveran and Mesnil, *op. cit.*)

In human Trypanosomiasis arsenical compounds have been often tried and have yielded only a passing amelioration, but in general the doses prescribed have been too feeble. Judging by the results of experiments on animals, one may say that the method which consists in giving small daily doses of arsenious acid (the method most frequently adopted in the treatment of human Trypanosomiasis) is bad, and that it is preferable to administer large doses at longer intervals.

Writers are all agreed that human Trypanosomiasis is always fatal as soon as the nervous symptoms declare themselves, but before the appearance of these symptoms there is a period, more or less long, during which the Trypanosomes, in small number in the blood, produce but few morbid troubles. In this first phase it is probable that the infection produced by *Tr. gambiense* is curable in the human subject as it is in many species of animals, and that arsenious acid may contribute to a cure.

Good hygienic conditions and abundant food are also important factors in the treatment of Trypanosomiasis; in Africa the "sleeping sickness" rages with a peculiar intensity among the miserable Negro labourers, overworked and ill-fed. (Note—Christy, Rep. of the Sleeping Sickness Comm., Nov. 1903: in Uganda the epidemic of Trypanosomiasis has been greatly aggravated by famine.) The same thing is observed among animals, those that have some defect or some cause of enfeeblement are more strongly infected than those which are in good condition and are supplied with abundant food.—*Comptes Rendus*, tome cxxxviii. p. 450 (22 Feb., 1904).

Relations between the Development of the Tracheal Apparatus and the Metamorphoses of Insects. By JULES ANGLAS.

The phenomena of internal metamorphosis have in Insects a strict relation to the development of the respiratory apparatus.

The metamorphoses properly so-called, characterized by the phenomena of histolysis followed by histogenesis, bear, moreover, even among the Holometabolids, only on the middle portion of the intestine, the muscles, and sometimes on the tracheal apparatus itself.

In the Hymenoptera that I have studied (Wasps, Bees) these